

### **Amendments to the Claims**

#### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-91. **[Canceled]**

Claim 92. **[New]** A polypeptide comprising a variant Fc region, wherein said variant Fc region differs from a wild-type Fc region by comprising at least an amino acid modification at position 396 relative to said wild-type Fc region, wherein said polypeptide binds an Fc $\gamma$ R with an increased affinity relative to a polypeptide comprising said wild-type Fc region.

Claim 93. **[New]** The polypeptide of claim 92, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) at position 210; 215; 217; 246; 250; 255; 268; 288; 290; or 419 of said wild-type Fc region.

Claim 94. **[New]** The polypeptide of claim 92, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) of said wild-type Fc region selected from the group consisting of: 210M; 217S; 227S; 240A; 242F; 244H; 246T; 247S; 248M; 250A; 250S; 255I; 255L; 258D; 268D; 268N; 303I; 305L; 323I; 326I; 334N; 358P; 370E; 375C; 379M; 384K; 392T; 400F; 410H; 419H; 419L; or 427A.

Claim 95. **[New]** The polypeptide of claim 92, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid

modification(s) of said wild-type Fc region selected from the group consisting of:

- (A) 221E; 270E; 308A, 311H and 402D;
- (B) 319F and 352L;
- (C) 288R; 307A; and 344E;
- (D) 210M and 261N;
- and
- (E) 243L; 305I; 378D; and 404S.

Claim 96. [New] The polypeptide of any of claims 92-95, wherein said Fc $\gamma$ R is Fc $\gamma$ RIIIA.

Claim 97. [New] The polypeptide of claim 96, wherein said variant Fc region of said polypeptide has decreased affinity for Fc $\gamma$ RIIB relative to said wild-type Fc region.

Claim 98. [New] The polypeptide of claim 97, wherein said variant Fc region comprises amino acid modifications of said wild-type Fc region selected from the group consisting of:

- (A) 221E; 270E; 308A; 311H; 396L and 402D;
- (B) 243L; 305I; 376D; 404S; and 396L;
- (C) 255I and 396L;
- (D) 370E and 396L.
- (E) 392T and 396L;
- and
- (F) 410H and 396L.

Claim 99. [New] The polypeptide of any of claims 92-95 wherein said wild-type Fc region is an Fc region of a human IgG Fc region.

Claim 100. [New] The polypeptide of claim 99, wherein said human IgG Fc region is a human IgG1, IgG2, IgG3, or IgG4 Fc region.

- Claim 101. [New] An antibody which comprises an antigen binding region and a variant Fc region, wherein said variant Fc region:
- (A) differs from a wild-type Fc region by comprising at least an amino acid modification at position 396 relative to said wild-type Fc region; and
  - (B) binds an Fc $\gamma$ R with an increased affinity relative to a said wild-type Fc region.
- Claim 102. [New] The antibody of claim 101, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) at position 210; 215; 217; 246; 250; 255; 268; 288; 290; or 419 of said wild-type Fc region.
- Claim 103. [New] The antibody of claim 101, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) of said wild-type Fc region selected from the group consisting of: 210M; 217S; 227S; 240A; 242F; 244H; 246T; 247S; 248M; 250A; 250S; 255I; 255L; 258D; 268D; 268N; 303I; 305L; 323I; 326I; 334N; 358P; 370E; 375C; 379M; 384K; 392T; 400F; 410H; 419H; 419L; or 427A.
- Claim 104. [New] The antibody of claim 101, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) of said wild-type Fc region selected from the group consisting of:
- (1) 221E; 270E; 308A, 311H and 402D;
  - (2) 319F and 352L;
  - (3) 288R; 307A; and 344E;
  - (4) 210M and 261N;
- and
- (5) 243L; 305I; 378D; and 404S.

- Claim 105. [New] The antibody of any of claims 101-104, wherein said Fc $\gamma$ R is Fc $\gamma$ RIIIA.
- Claim 106. [New] The antibody of claim 105, wherein said variant Fc region of said polypeptide has decreased affinity for Fc $\gamma$ RIIB relative to said wild-type Fc region.
- Claim 107. [New] The antibody of claim 106, wherein said variant Fc region comprises amino acid modifications of said wild-type Fc region selected from the group consisting of:
- (1) 221E; 270E; 308A; 311H; 396L and 402D;
  - (2) 243L; 305I; 376D; 404S; and 396L;
  - (3) 255I and 396L;
  - (4) 370E and 396L.
  - (5) 392T and 396L;
- and
- (6) 410H and 396L.
- Claim 108. [New] The antibody of any of claims 101-104 wherein said wild-type Fc region is an Fc region of a human IgG Fc region.
- Claim 109. [New] The antibody of claim 108, wherein said human IgG Fc region is a human IgG1, IgG2, IgG3, or IgG4 Fc region.
- Claim 110. [New] The antibody of claim 108, wherein said variant Fc region of said antibody specifically binds Fc $\gamma$ RIIIA with at least two times greater affinity than the wild-type Fc region.
- Claim 111. [New] The antibody of claim 101-104, wherein said antigen binding region binds a cancer antigen or an antigen associated with an infectious disease.

- Claim 112. [New] The antibody of claim 111, wherein said antibody binds a cancer antigen and mediates antibody dependent cell mediated cytotoxicity 2-fold more effectively than an antibody comprising said wild-type Fc region.
- Claim 113. [New] The antibody of claim 111, wherein said antibody binds a cancer antigen and said cancer antigen is HER-2/neu, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, MUM-1, CDK4, MUC-1, N-acetylglucosaminyltransferase, p15, beta-catenin, human papillomavirus-E6, or human papillomavirus-E7.
- Claim 114. [New] A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 111, and a pharmaceutically acceptable carrier.
- Claim 115. [New] The pharmaceutical composition of claim 114, wherein said antibody binds a cancer antigen and said composition further comprises an additional anti-cancer agent selected from the group consisting of a chemotherapeutic agent, a radiation therapeutic agent, a hormonal therapeutic agent, and an immunotherapeutic agent.
- Claim 116. [New] A method of treating cancer in a patient having a cancer characterized by a cancer antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody which comprises an antigen binding region and a variant Fc region, wherein said variant Fc region:
- (A) differs from a wild-type Fc region by comprising at least an amino acid modification at position 396 relative to said wild-type Fc region; and
  - (B) binds an FcγR with an increased affinity relative to a said wild-type Fc region.

- Claim 117. [New] The method of claim 116, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) at position 210; 215; 217; 246; 250; 255; 268; 288; 290; or 419 of said wild-type Fc region.
- Claim 118. [New] The method of claim 116, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) of said wild-type Fc region selected from the group consisting of: 210M; 217S; 227S; 240A; 242F; 244H; 246T; 247S; 248M; 250A; 250S; 255I; 255L; 258D; 268D; 268N; 303I; 305L; 323I; 326I; 334N; 358P; 370E; 375C; 379M; 384K; 392T; 400F; 410H; 419H; 419L; or 427A.
- Claim 119. [New] The method of claim 116, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) of said wild-type Fc region selected from the group consisting of:
- (1) 221E; 270E; 308A, 311H and 402D;
  - (2) 319F and 352L;
  - (3) 288R; 307A; and 344E;
  - (4) 210M and 261N;
- and
- (5) 243L; 305I; 378D; and 404S.
- Claim 120. [New] The method of claim 116, wherein said variant Fc region comprises amino acid modifications of said wild-type Fc region selected from the group consisting of:
- (1) 221E; 270E; 308A; 311H; 396L and 402D;
  - (2) 243L; 305I; 376D; 404S; and 396L;
  - (3) 255I and 396L;
  - (4) 370E and 396L.

- (5) 392T and 396L;  
and
- (6) 410H and 396L.

- Claim 121. [New] The method of any of claims 116-120 wherein said wild-type Fc region is an Fc region of a human IgG Fc region.
- Claim 122. [New] The method of claim 121, wherein said human IgG Fc region is a human IgG1, IgG2, IgG3, or IgG4 Fc region.
- Claim 123. [New] The method of claim 121, wherein said variant Fc region of said antibody specifically binds FcγRIIIA with at least two times greater affinity than the wild-type Fc region.
- Claim 124. [New] The method of claim 116, wherein said therapeutic antibody mediates antibody dependent cell mediated cytotoxicity 2-fold more effectively than an antibody comprising said wild-type Fc region.
- Claim 125. [New] The method of claim 116, wherein said cancer antigen is HER-2/neu, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, MUM-1, CDK4, MUC-1, N-acetylglucosaminyltransferase, p15, beta-catenin, human papillomavirus-E6, or human papillomavirus-E7.
- Claim 126. [New] A method of treating an infectious disease in a patient having an infectious disease characterized by a disease-associated antigen, said method comprising administering to said patient a therapeutically effective amount of an antibody which comprises an antigen binding region and a variant Fc region, wherein said variant Fc region:
- (A) differs from a wild-type Fc region by comprising at least an amino acid modification at position 396 relative to said wild-type Fc region; and

- (B) binds an FcγR with an increased affinity relative to a said wild-type Fc region.

Claim 127. [New] The method of claim 126, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) at position 210; 215; 217; 246; 250; 255; 268; 288; 290; or 419 of said wild-type Fc region.

Claim 128. [New] The method of claim 126, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) of said wild-type Fc region selected from the group consisting of: 210M; 217S; 227S; 240A; 242F; 244H; 246T; 247S; 248M; 250A; 250S; 255I; 255L; 258D; 268D; 268N; 303I; 305L; 323I; 326I; 334N; 358P; 370E; 375C; 379M; 384K; 392T; 400F; 410H; 419H; 419L; or 427A.

Claim 129. [New] The method of claim 126, wherein said variant Fc region differs from said wild-type Fc region in comprising additional amino acid modification(s) of said wild-type Fc region selected from the group consisting of:

- (1) 221E; 270E; 308A, 311H and 402D;
  - (2) 319F and 352L;
  - (3) 288R; 307A; and 344E;
  - (4) 210M and 261N;
- and
- (5) 243L; 305I; 378D; and 404S.

Claim 130. [New] The method of claim 126, wherein said variant Fc region comprises amino acid modifications of said wild-type Fc region selected from the group consisting of:

- (1) 221E; 270E; 308A; 311H; 396L and 402D;
- (2) 243L; 305I; 376D; 404S; and 396L;



- (3) 255I and 396L;
- (4) 370E and 396L.
- (5) 392T and 396L;
- and
- (6) 410H and 396L.

Claim 131. [New] The method of any of claims 126-130 wherein said wild-type Fc region is an Fc region of a human IgG Fc region.

Claim 132. [New] The method of claim 131, wherein said human IgG Fc region is a human IgG1, IgG2, IgG3, or IgG4 Fc region.